4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-D-0053]

Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers; Revised Draft Guidance for Industry; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a revised draft guidance for industry entitled "Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers." This revised draft guidance, when finalized, will provide FDA's current thinking on common questions regarding certain communications by *firms* to *health care providers* (*HCPs*) of scientific information on *unapproved use(s)* of *approved/cleared medical products* (the scope of the italicized terms is further explained in the revised draft guidance). This revised guidance supersedes the revised draft guidance entitled "Distributing Scientific and Medical Publications on Unapproved New Uses--Recommended Practices" issued in 2014 (2014 revised draft guidance).

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance. Submit electronic or written comments on the proposed collection of information in the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF THE PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2008-D-0053 for "Communications From Firms to Health Care Providers Regarding Scientific Information on

Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002; the Office of Policy, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5431, Silver Spring, MD 20993-0002; or the Policy and Regulations Staff, (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your request. See the SUPPLEMENTARY INFORMATION section for information on electronic access to the draft guidance.

FOR FURTHER INFORMATION CONTACT: *With regard to the draft guidance*: Kathleen David, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Room 3203, Silver Spring, MD 20993-0002, 301-796-1200; Anne Taylor, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911; Ana Loloei, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5504, Silver Spring, MD 20993-0002, 301-796-8774; Office of Surveillance and Compliance, Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl. (HFV-6), Rockville, MD 20855, 240-402-7082; Julie Finegan, Office of Policy, Office of the Commissioner, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 4252, Silver Spring, MD 20993-0002, 301-827-4830.

With regard to the proposed collection of information: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled "Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers." Specifically, this revised draft guidance relates to *firms* sharing the following types of communications with *HCPs*:

- published scientific or medical journal articles (reprints),
- published clinical reference resources, as follows:
  - clinical practice guidelines (CPGs),
  - scientific or medical reference texts (reference texts),
  - materials from independent clinical practice resources, and
- firm-generated presentations of scientific information from an accompanying published reprint.

For the purposes of this revised draft guidance, these specific types of communications from *firms* to *HCPs* of *scientific information on unapproved uses* (SIUU) of *approved/cleared medical products* in combination with the disclosures recommended in the guidance are referred to as "*SIUU communications*." We acknowledge that *firms* share *SIUU communications* through different media (e.g., paper, digital), and the recommendations in this guidance apply regardless of the medium of the communication. Other communications by *firms* are not specifically addressed by this revised draft guidance, and we do not intend to convey any views on such communications in issuing this revised draft guidance.

This revised draft guidance represents a continuation of FDA's ongoing efforts to consider, develop, and refine its policies and recommendations relating to communications by *firms* about *unapproved uses* of their *approved/cleared medical products*. In 2009, FDA issued a final guidance for industry entitled "Good Reprint Practices for the Distribution of Medical

Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices" (74 FR 1694) to provide guidance to *firms* on distributing "journal articles" and "scientific or medical reference publications." Then, FDA issued the 2014 revised draft guidance (79 FR 11793) to clarify the Agency's position on *firms* disseminating scientific or medical reference texts and CPGs that include information on *unapproved uses* of the *firm's* medical products and to provide additional explanation on these topics.

In developing this revised draft guidance, FDA considered stakeholder feedback, including comments received on the 2014 revised draft guidance. This revised draft guidance will supersede the 2014 revised draft guidance. Changes include a revised title, a question-and-answer format, and certain changes in scope.

The Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and their implementing regulations prohibit, among other things, the introduction (or causing the introduction) into interstate commerce of a medical product that fails to comply with applicable premarket requirements or is otherwise misbranded or adulterated. This prohibition includes introducing (or causing the introduction) into interstate commerce a medical product that is intended for a use that has not been approved or cleared by FDA, even if that same product is approved or cleared for a different use. These premarket requirements further multiple important government interests and distributing *approved/cleared medical products* for *unapproved uses* can undermine these interests. In certain circumstances, however, *HCPs* may be interested in scientific information about *unapproved uses* of *approved/cleared medical products* to inform clinical practice decisions for the care of an individual patient. In developing this draft guidance, FDA has sought to strike a careful balance between supporting *HCP* interest in scientific information about *unapproved uses* of *approved/cleared medical products* to inform clinical practice decisions for the care of an individual patient, and mitigating the potential that the government interests advanced by these statutory requirements will be undermined.

In light of those goals, FDA believes it is critical that *SIUU communications* be truthful, non-misleading, factual and unbiased and provide all information necessary for *HCPs* to interpret the strengths and weaknesses and validity and utility of the information in the *SIUU communication*. In addition, any study or analysis described in a *source publication* that serves as the basis for an *SIUU communication* should be scientifically sound. The studies or analyses should also provide information that is relevant to *HCPs* engaged in making clinical practice decisions for the care of an individual patient (as used in this revised draft guidance, "clinically relevant"). The manner of presentation of *SIUU communications* is also critical to consider. This revised draft guidance provides recommendations addressing all of these considerations.

If a *firm* shares an *SIUU communication* with *HCPs* in a manner that is consistent with the recommendations in this revised draft guidance, FDA does not intend to use such communication standing alone as evidence of a new intended use.

This revised draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The revised draft guidance, when finalized, will represent the current thinking of FDA on "Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

Under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to

provide a 60-day notice in the *Federal Register* concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Recommendations for Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities; and Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers

OMB Control Number 0910-0857--Revision

The revised draft guidance document, "Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers," discusses information disclosures that we recommend *firms* include in *SIUU communications* if the *firms* choose to publicly share such communications.

We estimate the burden of the information collection as follows:

Table 1.--Estimated Annual Third-Party Disclosure Burden[1]

Recommended Disclosure Activity; Guidance Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
A statement that the unapproved use(s) of the medical product has not been approved by FDA and that the safety and effectiveness of the medical product for the unapproved use(s) has not been established; Q2	1,008	30	30,240	0.1 (6 minutes)	3,024
A statement disclosing the FDA-approved use(s) of the medical product, including any limitations of use specified in the FDA-required labeling; Q2	1,008	27	27,216	0.1 (6 minutes)	2,721.6
A statement disclosing any limitations, restrictions, cautions, or warnings described in the FDA-required labeling about the unapproved use(s); Q2	1,008	5	5,040	0.2 (12 minutes)	1,008
A copy of the most current FDA-required labeling (or a mechanism for obtaining this labeling, as appropriate); Q2	1,008	27	27,216	0.1 (6 minutes)	2,721.6
A statement describing any contraindication(s) in the FDA-required labeling for the medical product; Q2	1,008	3	3,024	0.1 (6 minutes)	302.4
A statement describing any serious, life-threatening, or fatal risks posed by the medical product that are in the FDA-required labeling for the medical product or known by the firm and that are relevant to the unapproved use(s). If a risk evaluation and mitigation strategy (REMS) has been established under 21 U.S.C. 355-1, the statement should disclose that fact and should describe the goal(s) of the REMS; Q2	1,008	25	25,200	0.2 (12 minutes)	5,040
A statement identifying any authors, editors, or other contributors to publication(s) included in the SIUU communication who were employees of or consultants to or who received compensation from the firm at the time of writing, editing, or contributing to the publication, to the extent that a firm acting reasonably would know of such relationship; Q2	1,008	20	20,160	0.2 (12 minutes)	4,032

Table 1.--Estimated Annual Third-Party Disclosure Burden[1]

Recommended Disclosure Activity; Guidance Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
In the case of an SIUU communication that is based on a source publication that is primarily focused on a particular scientific study or studies, for each such study where the following information is not included in the publication, provide a description of: -All material aspects of study design, methodology, and results; -All material limitations related to the study design, methodology, and results; and -When applicable, conclusions from other relevant studies that are contrary to, or cast doubt on, the results shared, including citations for any such studies; Q2	1,008	20	20,160	2.75	55,440
The publication date of any referenced or included publication(s) (if not specified in the publication or citation); Q2	1,008	3	3,024	0.1 (6 minutes)	302.4
When firms share an SIUU communication in the form of an unabridged CPG or reference text in its entirety that discusses a wide range of medical products and that discussion is not primarily focused on one or more of a firm's medical products, the firm should include, in lieu of some of the specific disclosures listed above, a more general statement in the SIUU communication, such as "This [CPG/reference text] describes some uses of medical products that are not approved by the FDA and the safety and effectiveness of any unapproved use(s) have not been established."; Q4	1,008	3	3,024	0.1 (6 minutes)	302.4
When firms share an SIUU communication in the form of a firm-generated presentation of scientific information from an accompanying reprint that SIUU communication should clearly disclose what portions of the communication are firm-generated; Q4	1,008	10	10,080	0.1 (6 minutes)	1,008
Total			174,384		75,902.4

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Based on a current listing of firms promoting approved/cleared human and animal drug products (747), combined with an estimated number of device firms marketing products (261), we assume 1,008 firms ("number of respondents" in table 1) may each choose to publicly share

30 *SIUU communications* annually. Our estimate of the burden per disclosure (2.5 hours) reflects what we believe is the average burden based on the number and content and complexity of disclosures as recommended in the guidance.

III. Request for Comment on Other Issues for Consideration

FDA is interested in additional matters related to communications by *firms* about scientific information on *unapproved use(s)* of *approved/cleared medical products*. This revised draft guidance pertains to these communications by *firms* to *HCPs* engaged in making clinical practice decisions for the care of an individual patient. FDA is specifically seeking input on the following:

1. What considerations, if any, exist that are unique to communications of scientific information about *unapproved use(s)* of *approved/cleared medical products* by *firms* to researchers (including *HCPs* working in their capacity as researchers)?
2. What other factors should *firms* consider when sharing firm-generated presentations (as described in the draft guidance) to ensure that presentations are truthful, non-misleading, factual and unbiased and provide all information necessary for *HCPs* to interpret the strengths and weaknesses and validity and utility of the presented information?

IV. Electronic Access

Persons with access to the internet may obtain an electronic version of the draft guidance at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances, https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm, https://www.fda.gov/animal-veterinary/guidance-regulations/guidance-industry, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.regulations.gov.

Dated: October 18, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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